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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,926	01/16/2002	Jeffrey R. Sampson	2003309-0027 (Agilent 10	1042
7590	06/06/2006		EXAMINER TUNG, JOYCE	
AGILENT TECHNOLOGIES, INC. Legal Department, DL429 Intellectual Property Administration P.O. Box 7599 Loveland, CO 80537-0599			ART UNIT	PAPER NUMBER
			1637	
DATE MAILED: 06/06/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/052,926	SAMPSON, JEFFREY R.	
	Examiner	Art Unit	
	Joyce Tung	1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 16 May 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: 1-35,67-101 and 144-149.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: please see the attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____.
13. ☐ Other: _____.

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The applicant's amendment filed 5/16/06 to the Office action has been entered. Claims 1-35, 67-101 and 144-149 are pending.

1. Claims 1-34, 67-100 and 144-149 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Baldarelli et al. (6,015,714, issued Jan. 18, 2000) in view of Kool (5,714,320, issued Feb. 3, 1998).

Baldarelli et al. disclose a method for sequencing nucleic acid polymer. The description of the method of Baldarelli et al. as listed in claims 1-24 (See Abstract and column 23-24, claims 1-24). Modified base are available including methylated bases (See column 8, lines 44-45). In order to identify the monomers, condition should be appropriate to avoid secondary structure in the polymer to be sequenced (See column 8, lines 53-54).

Baldarelli et al. do not disclose using a circular template, the nucleic acid molecule containing modified nucleotides, which are modified adenosine, modified thymine, modified guanosine and modified cytosine.

Kool et al. disclose a method for synthesis and amplification of DNA and RNA oligonucleotide which involves using circular oligonucleotide template and the nucleotide triphosphates is modified, 2-amino-adenosine-TP (See column 13, lines 50-67). The method uses enzymatic synthesis, which is polymerase enzyme (See column 5, lines 31-46). The teachings of Kool et al. suggest that the synthesized nucleic acid molecules contain modified nucleotides. The products generated from the method include a linear multimer having the desired sequence (See column 14, lines 29-38).

Although the modified nucleotide used in the method of Kool et al. is to make cleavage site (See column 30, lines 57-58), while in the instant invention, the modified nucleotide of the

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synthesized nucleic acid molecule is to reduce secondary structures in the synthesized nucleic acid, the elements used in the synthesis of nucleic acid are the same.

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the method of Kool et al. to enzymatically synthesize nucleic acid molecule for the sequencing method of Baldarelli et al. because the method of Kool is directed to efficient, low-cost and large-scale synthesis of linear and circular oligonucleotide (See column 1, lines 21-25). It would have prima facie obvious to provide a nucleic acid molecule with at least one repeat of a nucleotide sequence to be determined, wherein the nucleic acid molecule is enzymatically synthesized using a circular template and the nucleic acid molecule contains modified nucleotides.

The response argues that Baldarelli et al. do not disclose generating nucleic acid polymers having repeats. Kool, discloses a method for synthesis and amplification of DNA and RNA oligonucleotide, which involves using circular oligonucleotide template. By doing so, one repeat of a nucleotide sequence is produced and multiple amplified copies of a single nucleic acid of interest are produced (See fig. 2).

The response additionally argues that Baldarelli et al. do not disclose the use of modified bases. However, Kool et al. disclose the modified nucleotide used in the method of Kool et al. is to make a cleavage site (See column 30, lines 57-58), while in the instant invention, the modified nucleotide of the synthesized nucleic acid molecule is to reduce secondary structures in the synthesized nucleic acid. Thus, both the claimed limitations and the invention of Kool et al. apply the modified nucleotide in the synthesized nucleic acid. The effect of using the

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modified nucleotide is different. The effect of using the modified nucleotide has no patentable weight.

The response argues that the reference of Kool is not combinable with Baldarelli et al. because synthesis and sequencing of nucleic acids are diverse as to be considered non-analogous. However, both references are used in molecular biology. Thus they are analogous references. Therefore, the rejection is maintained.

2. Claims 35 and 101 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Baldarelli et al. (6,015,714, issued Jan. 18, 2000) in view of Kool (5,714,320, issued Feb. 3, 1998) as applied to claims 1-34, and 67-100 above, and further in view of Thorp et al. (5,871,918, issued Feb. 16, 1999).

The references of Baldarelli et al. and Kool set forth in section 1 above do not disclose analyzing nucleic acid by electron tunneling.

Thorp et al. disclose a method of detecting a nucleic acid by using electron tunneling (See column 9, lines 30-55). The method may be used in a variety of applications, including DNA sequencing (See the Abstract).

One of ordinary skill in the art would have been motivated to modify the method of Baldarelli et al. by applying electron tunneling as taught by Thorp et al. since the electron tunneling is applied to DNA sequencing. It would have been prima facie obvious to apply the electron tunneling to the method of Baldarelli et al. to make the instant invention for sequencing DNA.

Since there is no specific argument regarding this rejection, the rejection is maintained.

New Ground of Rejection

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 148-149 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 148 is vague and indefinite because it is unclear whether the newly added claim has further limitations to claim 1. It appears that claim 1 requires the step of producing the provided nucleic acid by enzymatically synthesizing the nucleic acid using a circular template (See claim 1). Clarification is required.

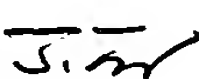
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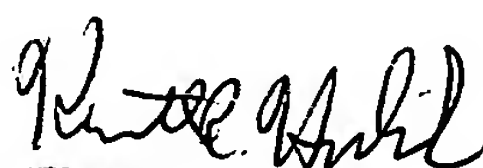
5. No claims are allowable.
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joyce Tung 
May 30, 2006


KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER

6/1/06